

affinity for the first surface lower than the affinity of the displaceable moiety for the analyte of interest;

exposing the first surface to a sample comprising the analyte of interest, whereby the analyte of interest specifically displaces the displaceable moiety from the first surface;

causing the displaceable moiety displaced from the first surface to contact a second surface bearing a capture moiety which specifically binds to the displaceable moiety, so as to capture the displaceable moiety on the second surface, said capture generating a species capable of producing a detectable signal; and

treating the species capable of producing a detectable signal to generate said signal and detecting the signal; wherein said detection is performed by means other than Surface Plasmon Resonance, and wherein the detectable signal cannot be [is not] generated unless and until the displaceable moiety is captured on the second surface [whereupon said detectable signal indicating detection of analyte in said assay is generated].

Please amend claim 7 to read as follows:

7. (twice amended) A method according to claim 1, wherein the first surface comprises a plurality of intervening molecules which bind relatively loosely to the displaceable moiety, such that the binding affinity of the intervening [moiety] molecules for the analyte of interest is greater than that of the displaceable moiety for the intervening [moiety] molecules.

REMARKS

This is in response to the Official Action mailed July 22, 2002 for the above-captioned application. Reconsideration of the application, as amended, is respectfully requested.

Claims 1-3, 5-16, 22 and 23 are pending and under examination. Claim 1 has been amended to more clearly define the broad scope of the invention and to clearly establish that the capture of displaceable moiety by the second surface results in a species which can generate a detectable signal, but which may not do so spontaneously on capture. This amendment to the claims is clearly supported in the specification, for example in the embodiment described on page

7 of the application wherein there is binding of a fluorophore which is capable of being stimulated by an evanescent wave. Binding does not generate the signal. It is the binding event that causes a change in the properties of the fluorophore. The signal is generated as a consequence of stimulation by an evanescent wave.

The Examiner rejected claims 7 and 12 under 35 USC § 112, second paragraph. Claim 7 has been amended to correct the error noted by the Examiner. With respect to claim 12, Applicants respectfully traverse the rejection, and request either withdrawal of the rejection or clarification. The Examiner has rejected claim 12 asserting that the term "properties" renders the claim indefinite. Applicants addressed this argument in the Preliminary Amendment, but the Examiner has not responded to these arguments. Thus, they are repeated here.

Claim 12 is a dependent claim which recites that the capture of the displaceable moiety by the capture moiety directly modulates the "electrochemical properties" of the displaceable moiety. The Examiner has asserted without explanation that the use of the term "properties" renders the claims indefinite. Thus, the Examiner has made only a conclusory allegation and has not met the burden of establishing that a person skilled in the art would be unable to ascertain the scope of the claims (*Ex parte Cordova*, 10 U.S.P.Q. 2d 1949, 1952 (POBAI 1989))("it is incumbent on the Examiner to establish that one having ordinary skill in the art would not have been able to determine the scope of protection defined by the claim when read in light of the specification"). Furthermore, Applicants respectfully submit that there is nothing unclear or ambiguous about the term "electrochemical properties" which is the term that actually appears in claim 12. Persons skilled in the art would understand the plain language of claim 12 to mean that the binding of the displaceable moiety results in a change in the properties of the capture moiety which can be measured using electrochemical techniques such as amperometry, voltametry or coulombetry (as opposed to detecting color for example). Such a change might be a change in the redox potential (the amount of potential difference necessary to cause an oxidation or reduction reaction), or a change in the conductivity/resistance of the material or some similar change. Furthermore, this is precisely the definition which is provided in the specification on Page 8. Thus, Applicants submit that rejection of claim 12 under 35 USC § 112,

second paragraph is in error and should be withdrawn. Alternatively, the Examiner is requested to explain **why** the language of claim 12 would be unclear to a person skilled in the art.

On the merits, the Examiner rejected claims 1-3, 7-10 and 13-16 as anticipated by Schramm et al. (WO 91/05262). Claim 1, upon which all of the rejected claims depend, requires the generation and detection of a signal. However, as specified in the claim, "the detectable signal cannot be generated unless and until the displaceable moiety is captured on the second surface." The Examiner argues that this limitation is met by Schramm, et al., because it teaches that "upon being bound to the second surface, the displaced moiety converts the substrate into a colored product (in an enzyme assay), thus a colored signal is generated." (Office Action, Page 6). Applicants respectfully point out, however, that the signal generating moiety in this embodiment in Schramm is an enzyme-analyte conjugate, and that this conjugate produces a detectable signal in the presence of appropriate added substrate, whether bound to a solid surface or not, and regardless of the location in which it is bound. The same is true of the other signal generating means disclosed in Schramm, i.e., "enzymes, fluorescent molecules, ultraviolet absorbent agents, and other compounds capable of conjugation with the analyte without deletion of the ability to generate the signal." (Page 9, lines 9-14). Thus, far from having the signal-generating ability be one which is dependent on binding, Schramm teaches the signal-generating ability to be a necessary inherent characteristic of the signal generating means which must not be eliminated by binding.

Applicants further note that in Schramm, "the signal generator molecule generates a detectable signal distinguishing binding thereof at the first **or** second binding means." (Page 7, lines 9-11). Thus, in Schramm, it is not the generation of a signal, but the location of the signal which is diagnostic, since the signal may be developed at either binding location. Furthermore, detectable signal is generated in Schramm whether analyte is present or not. (See Page 10, line 26-page 11, line 25). This is not comparable to nor suggestive of the claimed invention, in which binding of the displaceable moiety at the second surface is a necessary predicate to the formation of a detectable signal. Thus, Applicants do not see how the device of Schramm meets the limitations of claim 1. Absent a complete teaching of every element, there can be no anticipation.

The Examiner also rejected claims 1-3, 7-8, 11-12 and 14-16 as anticipated by Partin et al (US 5,082,630). In Partin, the presence of a drug is detected by means of a reduction in fluorescence signal intensity when fluorescently labeled drug is displaced from a detection site. The fluorescent signal is not a signal which can be generated only when sample is bound, since the fluorescence which is observed (i.e., that from the label on non-displaced drug) is present whether or not the drug is bound. Thus, the limitation in claim 1, is not met by Partin either.

Applicants further point out that the application of this rejection to claim 12 appears to be in error. Claim 12 recites that the capture of the displaceable moiety directly modulates an **electrochemical** property of the capture moiety. In Partin, the signal which the Examiner has referred to is a fluorescent light emission. There is no electrochemical property mentioned in the reference. Thus, the citation of this reference as anticipating claim 12 is not understood.

Claims 5, 6 and 22 stand rejected as obvious over Schramm et al. or Partin et al. These claims are dependent on claim 1. In making the rejection, the Examiner assumes that the anticipation rejections are correct. As pointed out above, however, there are differences between the claimed invention which the Examiner has not appreciated. Thus, the Examiner has not indicated how these differences would be suggested by the cited art. Accordingly, Applicants submit that claims 5, 6 and 22 are allowable with the claims on which they depend.

In view of the foregoing arguments, Applicants submit that all claims are in form for allowance. Favorable reconsideration and allowance of all claims are respectfully urged.

Respectfully Submitted,



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